MedicalXpress

Molecular change may reveal risk of leukemia relapse

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Researchers may have discovered a better way to distinguish acute leukemia patients who require aggressive treatment to prevent recurrence from those who need only standard therapy for cure. The study is published in the May 1 issue of the *New England Journal of Medicine* with an accompanying editorial.

Researchers say that changes in levels of microRNAs, tiny molecules used by cells to help control the kinds and amount of proteins they make, might predict the risk of relapse in many adults diagnosed with acute myeloid leukemia (AML). All patients in the study had leukemia cells with normal-looking chromosomes.

The research also shows that the microRNAs involved in these AML patients regulate genes involved in inflammation and immune responses, providing new insights into possible causes of the disease.

The study was led by researchers at the Ohio State University Comprehensive Cancer Center.

“This is the first evidence linking changes in levels of microRNAs with the outcome of AML patients who lack the chromosome abnormalities that we commonly use to predict the cure or relapse of the disease,” says study co-leader Dr. Guido Marcucci, associate professor of medicine at Ohio State’s Comprehensive Cancer Center. “It provides a new tool for a personalized approach to the diagnosis and treatment of cancer.”

The study also points to the possible role played by abnormally triggered mechanisms of inflammation in the transformation of normal cells into AML cells, Marcucci notes. “In the future, we may find it possible to make leukemia cells more sensitive to therapy by replacing microRNAs that are too low or decreasing those that are too high.”

“If validated in a large prospective study, these findings could improve our ability to predict individual patient outcomes and identify the most effective therapy, and lead to new targeted therapies for leukemia,” says study leader Dr. Clara D. Bloomfield, an international AML authority at Ohio State’s Comprehensive Cancer Center and the William G. Pace III Professor of Cancer Research.

About 13,300 new cases of AML and 8,200 deaths from the disease are expected this year in the United States.

In about half of cases, patients’ leukemia cells have chromosome changes that help doctors determine whether standard therapy will suffice to prevent recurrence, or whether the individual needs aggressive treatment such as a stem-cell transplant or an experimental therapy.

The remaining patients have leukemia cells with chromosomes that look normal. Determining the best therapy for these individuals is much more difficult.

Recent research has identified changes within genes – mutations – that may help doctors identify which patients with normal-looking chromosomes have a high or low risk of relapse if given standard chemotherapy.

The new retrospective study suggests that changes in microRNA patterns might also predict relapse risk in these AML patients.

For this study, Marcucci, Bloomfield and colleagues began by measuring microRNA levels in blood samples collected from 64 AML patients under age 60 whose leukemia cells had normal-looking chromosome. The cells also had two gene markers indicating that the patients had a high risk of relapse.

All the patients had been treated through a clinical trial sponsored by the Cancer and Leukemia Group B (CALGB), a national clinical cooperative group.

This analysis revealed that abnormal levels of members of seven different families of microRNAs were associated with recurrence. The researchers then validated this molecular signature in a second group of 55 similar patients who had received identical therapy through a different CALGB trial.

High levels of members of six microRNA families were associated with greater recurrence risk, while high levels of members of the microRNA-181 family were associated with lower recurrence risk.

In addition, the researchers used a computer program to predict which genes were targeted by these microRNAs (each type of microRNA can regulate several genes). Many of the genes are involved in certain immune responses, including those that regulate the production of a substance called interleukin-1 beta (IL-1b).

“In addition to its role in inflammation, IL-1b has also been implicated in the unregulated growth of leukemia cells and might now be considered a therapeutic target in AML,” says Marcucci.

“Overall our findings indicate that microRNAs might help distinguish which AML patients in this difficult diagnostic group need aggressive therapy from those who will do fine on standard therapy,” says

Bloomfield who is also a Distinguished University Professor and Senior Advisor to the Ohio State cancer program. “This could truly help advance personalized health care.”

Source: Ohio State University Medical Center

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